Characterization of the Dynamic Shear Properties of Hyaline Cartilage in vitro using MR Elastography

O. Lopez[1], K. K. Amrami[1], A. Manduca[1], and R. L. Ehman[1]
[1]Radiology, Mayo clinic, Rochester, MN, United States

Introduction

Early degenerative changes in hyaline cartilage due to osteoarthritis (OA) have long been correlated to loss of stiffness of the tissue, which results from deterioration of superficial collagen fibrils and depletion of proteoglycan (PG) content (1). This notion has driven the development of numerous approaches capable of characterizing changes in the mechanical properties of cartilage that may be indicative of early degeneration (2,9,10). Our previous work has demonstrated that a customized dynamic MR elastography (MRE) technique may provide a sensitive quantitative tool to characterize the structural and functional properties of hyaline cartilage samples (3-6). The technique combines application specific hardware and imaging methods capable of generating and visualizing shear waves in the kilohertz range that propagate through the thickness of a cartilage sample. The mechanical excitation used in dynamic MRE of cartilage is performed in the kilohertz range due to the technical limitations imposed by the small size (< 6 mm thick) and high shear stiffness (μ_s > 200 kPa) of the cartilage (8).

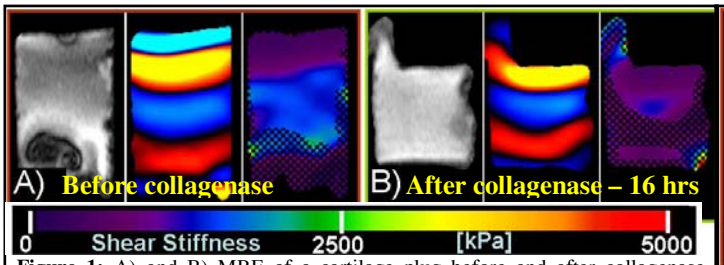
The purpose of the present study was to evaluate the feasibility of using the customized dynamic MRE technique to characterize structural changes in bovine hyaline cartilage induced by selective enzymatic degradation of collagen and PG constituents, as well as to evaluate the ability of the technique to quantify the frequency dependent response of normal cartilage to shear at frequencies in the kilohertz range.

Methods

Bovine cartilage plugs of 8 mm in diameter harvested from the femoral patellar groove (FPG) were used. Measurements of shear stiffness (μ_s) for each cartilage plug were derived from dynamic MRE data collected at 5000 Hz of shear excitation before and after 16 hours of selective enzymatic degradation. Cartilage plugs from the left knee joint (n = 7) were degraded using collagenase (30 U/mL) to disrupt the collagen fibril network. Similarly, cartilage plugs from the right knee joint (n = 7) were degraded using trypsin (100 µg/mL) to remove the proteoglycan content. The frequency dependent response of normal cartilage to shear was assessed by testing untreated cartilage plugs, harvested from the right (n = 6) and left (n = 6) FPGs, using dynamic MRE performed at 3000 Hz to 7000 Hz of mechanical excitation in increments of 1000 Hz. Estimates of μ_s measures from cartilage plugs were calculated by evaluating the spatial change of the phase in the temporal harmonic of the collected wave images at their respective mechanical excitation frequency (7). Typical acquisitions were made with a 1.5T imager using a GRE-MRE sequence with 60 motion-sensitization gradients (at 5000Hz), TR = 250 ms, TE = 24 ms, flip angle = 40 deg., slice thickness = 3 mm and FOV = 25x25 mm.

Results

Figure 1 shows results from dynamic MRE of cartilage plugs performed at 5000 Hz before and after 16 hours of enzymatic degradation. The elastograms in Figs.1-A, -B) and Figs.1-C, -D) demonstrate the ability of the technique to detect a significant decrease in μ_s after collagenase and trypsin treatments, respectively. The checkered board pattern on the elastograms represents low SNR regions which were not considered for estimating μ_s. Figures 2A and 2B show box plots of μ_s estimates made before and after cartilage plugs underwent 16 hours of enzymatic treatment with collagenase or trypsin, respectively. Measurements of μ_s after enzymatic treatment indicated that cartilage plugs were significantly softer (-37%) and (-28%) due to collagenase or trypsin treatments, respectively. Figure 3A) illustrates shortening of shear wavelength λ with increased frequency of mechanical excitation in a cartilage plug. Figure 3B) shows a systematic increasing trend of μ_s with frequency of mechanical excitation. Regression analysis showed a strong correlation (r = 0.9612) between the mechanical excitation frequency and the shear stiffness.



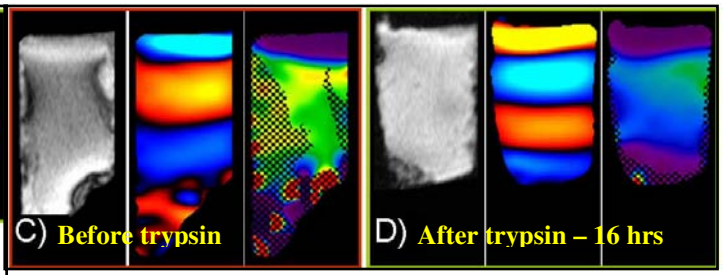


Figure 1: A) and B) MRE of a cartilage plug before and after collagenase treatment. C) and D) MRE of a cartilage plug before and after trypsin treatment. Each panel includes a GRE image of cartilage plug, a wave image at 5000 Hz and the calculated shear stiffness (μ_s) map (elastogram).

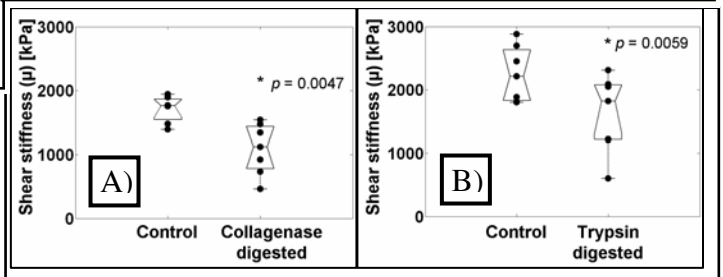
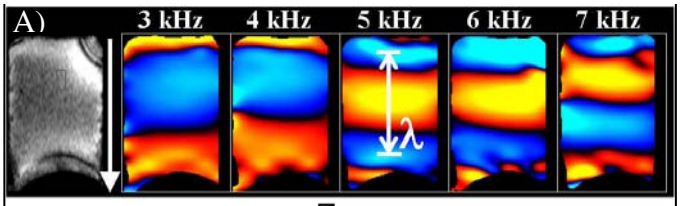


Figure 2: Measured μ_s for pre-treatment controls and enzyme treated cartilage: A) collagenase digested plugs (n = 7) and B) trypsin digested samples (n = 7).



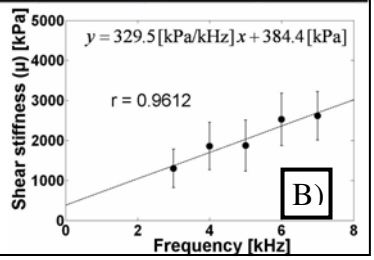


Figure 3: A) Wave image of a shear wave propagating at respective mechanical excitation frequencies through the thickness of a cartilage plug. B) Measured μ_s (mean ± SD) for untreated cartilage plugs (n = 12) as a function of mechanical excitation, 3000 to 7000 Hz.

Discussion

These results confirm that a customized dynamic MRE technique can be used as a sensitive tool to quantify changes in the dynamic shear properties of cartilage associated with disruptions to its macromolecular content. The technique also demonstrated sensitivity to the frequency dependent response of cartilage to shear, which lends itself useful to further characterize the tissue's viscoelastic behavior.

References

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